Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

Estimation of serum ferritin levels in newly diagnosed autoimmune hypothyroidism in Avadh region of UP, India

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Article History
Received: 17.09.2025
Revised: 08.10.2025
Accepted: 20.10.2025
Published: 31.10.2025

Abstract: Thyroid gland dysfunctions are among the most prevalent endocrine disorders in India. Although serum ferritin levels are known to be altered in hypothyroidism, limited data exist on ferritin status in autoimmune hypothyroidism. This study aimed to evaluate serum ferritin levels in patients with anti-TPO-positive autoimmune hypothyroidism. A comparative cross-sectional study was conducted at tertiary care hospital, Ayodhya, involving 80 newly diagnosed autoimmune hypothyroid patients (aged 25–55 years) and compared with 80 healthy controls. Biochemical parameters including fasting plasma glucose (FPG), thyroid profile, and serum ferritin were analysed. Data were statistically evaluated using SPSS version 29.0. The mean serum ferritin level was significantly lower in the hypothyroid group (17.15 ± 9.44 ng/mL) compared to controls (73.13 ± 44.46 ng/mL), with a p-value <0.0001. A strong negative correlation was found between TSH and serum ferritin levels (r = –0.68). These findings indicate a significant association between autoimmune hypothyroidism and reduced serum ferritin levels. This is the first study in the Ayodhya region of Eastern Uttar Pradesh to highlight this correlation, offering valuable insight into the relationship between thyroid function and iron metabolism.

Keywords: Hypothyroidism, ferritin, antithyroid peroxidase antibodies.

INTRODUCTION

Dysfunction and metabolic abnormalities of thyroid gland are among the most common disease of endocrine glands. [1] The burden of thyroid disease in general population of India is increasing day by day and thyroid dysfunctions are also the most frequent among the all endocrine diseases in India and worldwide.[2] Studies and various data clearly suggest that, globally 2 billion people are affected by thyroid dysfunction and in India approximately 42 million people suffer from thyroid abnormalities.[3] Thyroid hypofunction due to thyroid gland itself is known as primary hypothyroidism.[4] 99% of all hypothyroidism are primary hypothyroidism.[4] Thyroid hormone deficiency in hypothyroid patients causes slowing of a wide variety of metabolic processes, which results in reduce resting energy expenditure, decrease use of substrates and overall oxygen consumption.[1] The effect of reduce thermogenesis is related to cold intolerance of hypothyroid subjects. The decline in metabolic rate and substrate use contribute to decrease appetite and food intake. Studies suggest that the body weight is elevated on average by 10% because of an increase in body fat and increase retention of water and salt.[1] The incidence of hypothyroidism is estimated to be 4 to 5 per 1000 population per year for women and 0.6 to 0.9 per 1000 population per year for men.[5] The recent prevalence of overt hypothyroidism is approximately 1% to 2% in women and 0.1% in men.[6] Higher rates occur in older women, having high serum antithyroid peroxidase antibody.[7] Autoimmune thyroid dysfunction is associated with elevated serum level of antithyroid peroxidase antibody in 90-95% of patients.[8]

Serum ferritin is a storage form of iron and reflects body's stored iron level. Ferritin concentration in blood indicates the amount of iron available for use mainly in red blood cell production.[9] It is evident that, a low ferritin level than its normal reference is indicative of iron deficiency.[9] Evaluation of serum ferritin test is single reliable gold standard test to confirm iron deficiency as because significant fall in haemoglobin can not be detected until severe stage of iron deficiency.[10] Various studies have documented an association between thyroid abnormalities and serum ferritin expression.[11,12] Low level of serum ferritin is one of the most overlooked causes of reduced thyroid function. It was observed that T3 administer to hypothyroid individuals resulted a significance elevation in serum ferritin level, although underlying mechanism is poorly understood in humans.[13] Proper synthesis of thyroid hormones requires an iron containing vital enzyme thyroid peroxidase and in autoimmune thyroid dysfunction anti TPO antibodies produced against this enzyme. Iron inadequacy may affect proper functioning of TPO which may lead to thyroid dysfunction but there is no available literature in Indian population regarding the status of serum ferritin in autoimmune hypothyroidism to find out the relationship between anti TPO positive hypothyroidism and serum ferritin levels. Hence the present study is an endeavour to study the relation of serum ferritin levels and elevation in anti TPO assisted hypothyroidism.

MATERIAL AND METHODS

A comparative cross-sectional study was carried out in Biochemistry department in collaboration with General Medicine department for approximately 16 months duration from January 2024 to April 2025 in Rajshree Dashrat Autonomous State Medical College, Ayodhya. The study was performed on the patients attending the Medicine OPD. Ethical clearance was obtained from Institutional Ethical Committee. After calculating sample size 80 cases of newly diagnosed hypothyroid patients age group between 25 to 55 years were selected. Samples were taken in the basis of inclusion criteria. Inclusion criteria were newly diagnosed overt hypothyroid patients age group between 25 to 55 years and both sexes were included. Hypothyroid patients selection criteria of the cases were based on biochemical laboratory investigation and clinical sign and symptoms. Hypothyroid subjects were primarily diagnosed on the basis of total T3, T4 levels below the normal reference range and TSH above normal reference range. 80 age, sex matched apparently healthy subjects were selected as control whose thyroid profiles were within normal reference range. All the biochemical parameters (FPG, T3, T4, TSH, Anti TPO, Ferritin) were analysed at central Biochemistry laboratory. The following patients were excluded from our study setting. Subjects taking any kind of medication affecting thyroid hormone levels. Sub clinical hypothyroidism and secondary hypothyroidism. Diabetic, Tuberculosis, hypertension, cancer and known cases of HIV. Pregnant women and women with contraceptive pills. Obese subjects BMI> 35.

All the subjects were explained about aim and objective of the study. Written consents were obtained from all along with detail history. Height and weight of all the subjects were measured.

After overnight fast approximately 4 ml of blood was collected from an antecubital vein with full aseptic precaution without anticoagulant and allowed it to clot. Clotted blood was centrifuged and clear serum was collected. The serum was preserved at -20^{0}C until analysed. Thyroid profile (T3, T4, TSH,) test was done using Architech Chemiluminescence analysers I1SR1000. Anti TPO test was performed by ELISA method using Erba Lisa Scan EM instrument with Calbiotech ELISA kit. Serum ferritin analysed using by Architech chemi analyser (I1SR1000) by using Architech Ferritin reagent kit .Fasting plasma glucose was estimated by GOD-POD method by SelectraPro M autoanalyzer to rule out diabetic patients as exclusion criteria. All the test protocols were standardized and calibrated before quantization of all biochemical parameters as per NCCLS (National Committee for Clinical Laboratory Standards)[14] guidelines. Modified OSHA (Occupational safety and health act, 1970) guidelines were implemented in all steps of sample collection, processing & handling of bio-medical waste product[15].

Statistical analysis:

Statistical analysis was performed using SPSS version 29.0 All data was expressed as mean ± standard deviation. Comparison of serum levels of biochemical parameters between two groups was performed by unpaired Student 't' test. P value < 0.05 considered as statistically significant. Receiver Operating Characteristic curve (ROC) analysis was performed for serum ferritin to obtain cut off value with maximum sensitivity and specificity to find out diagnostic efficacy of serum ferritin.

RESULTS AND OBSERVATIONS:

The demographic characteristics and BMI of study population of hypothyroid subjects and control group is shown in Table -1. The mean age of hypothyroid patients was 40.86±7.58 years and control group was 40.15±7.42 years. The mean BMI of hypothyroid group was significantly elevated than the control group (BMI for hypothyroid 25.92±2.07; control 23.37± 1.54) with p value ,0.0001 which is statistically highly significant. Table 2 shows the age and sex distribution of hypothyroid case and control group. Thae maximum number of subjects in our study was between 41 to 45 years (n=23). Number of female patients (42/80) were more than that of males (38/80) in my study population.

Table -3 refer to normal values of T3, T4, TSH and anti TPO, and also observed values of hypothyroid group and control group. It was observed that TSH value was significantly raised in hypothyroid group (42.87±23.32 µIU/ml) with p value highly significant (< 0.0001). Mean anti TPO value of hypothyroid group was 125.35± 63.41 IU/ml as compared with control group it was found 11.41±6.66 IU/ml.

Plasma glucose level in both hypothyroid and control group was within normal reference range as all the non diabetic subjects were selected. Though in hypothyroid group the FPG was slightly raised (87.24±7.18) in comparison with control group (83.38±10.98). The mean serum ferritin level in hypothyroid group was 17.15±9.44 ng/ml and control group was 73.13 ±44.46 ng/ml as referred to table 4. On comparing with student 't' test, p value was < 0.0001 which is highly statistically significant. Figure-2 shows significant negative correlation of serum fettitin with TSH in hypothyroid patients with r value =-o.68

Figure -1 shows Box Plot demonstrating distribution of upper quartile, median and lower quartile of serum ferritin concentration (ng/ml) of hypothyroid and control group. Mean ± SD of hypothyroid group was 17.15±9.44 ng/ml. Median for hypothyroid group was 15.35. Mean ± SD of control group was 73.13 ±44.46 ng/ml and median for control group was 58.65. Figure-2 shows significant negative correlation of serum fettitin with TSH in hypothyroid patients with r value =-o.68

Table 1: Demographic characteristics of study population & BMI

Parameters	Controls (mean±SD)	Hypothyroid cases (mean±SD)
Age Yrs)	40.15±7.42	40.86±7.58
Mean age of Males	40.32±7.14	40.28±7.19
Mean age of Females	41.07±7.31	39.78±7.92
BMI	23.37± 1.54	25.92±2.07

Table 2: Age and Sex distribution of Hypothyroid cases and controls

Age (Years)	Controls (Total=80)		Hypothyroid cases (Total =80)	
	Males	Females	Males	Females
25-30	4	5	4	4
31-35	8	4	6	10
36-40	13	10	10	9
41-45	9	11	11	12
46-50	1	3	2	3
51-55	3	9	5	4
Total	38	42	38	42

Table 3: Thyroid profile in hypothyroid cases and control

Parameter	Normal range	Controls	Hypothyroid cases	p-value
T3 (ng/ml)	0.58-1.59	1.24±0.32	0.50±0.19	<0.0001
T4 (µg/dl)	4.8-11.7	7.12±2.01	2.87±1.26	<0.0001
TSH (µIU/ml)	0.35-5.9	2.66±1.29	42.87±23.32	<0.0001
Anti-TPO (IU/ml)	< 45 IU/ml	11.41±6.66	125.35± 63.41	<0.0001

Table 4: Comparison of biochemical parameters between two groups

Parameters	Controls (mean±SD)	Range (Control)	Hypothyroid cases (mean±SD)	Range (Hypothyroid cases)	p-value
Fasting Plasma glucose (mg/dl)	83.38±10.98	69-106	87.24±7.18	73-105	0.009
Serum Ferritin (ng/ml)	73.13 ±44.46	14-188.4	17.15±9.44	2.8-56.2	<0.0001

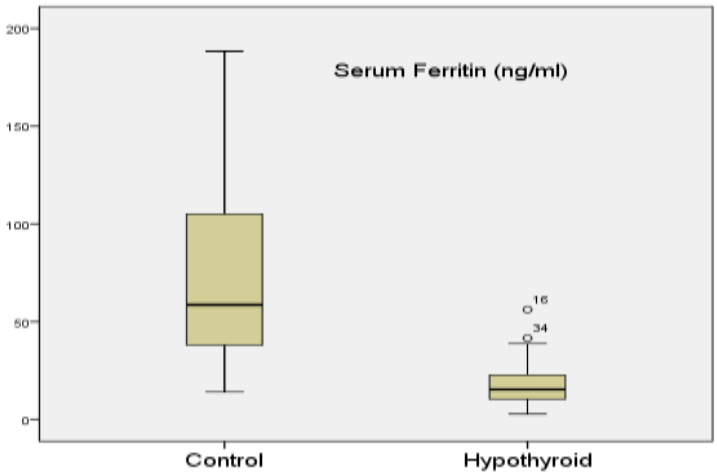

Fig-1: Box plot demonstrating upper quartile, median and lower quartile with max and min concentration values obtained for serum ferritin concentration (ng/ml)

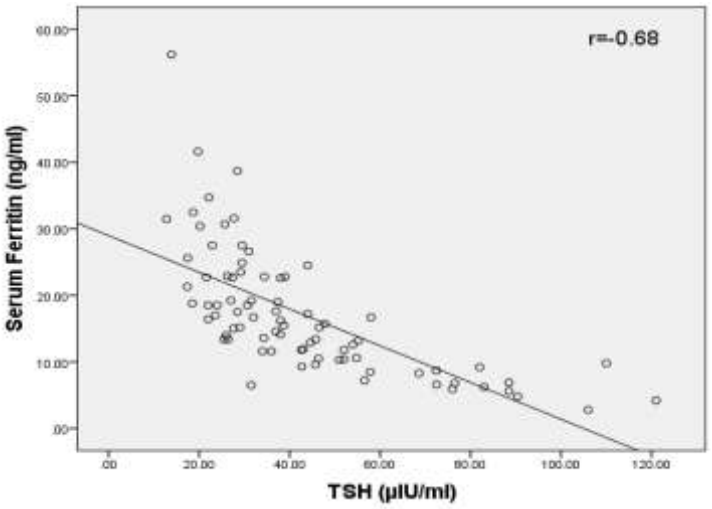

Fig-2: Correlation serum Ferritin with TSH in hypothyroid cases.

Fig-3 shows ROC curve analysis of serum ferritin concentration (ng/ml) in hypothyroid and control group. Area under curve was 0.947; standard error as per Hanley & McNeil was 0.016; 'p' value,0.00; sensitivity was 85% and specificity was 89% with best cut off value 26.95 ng/ml.

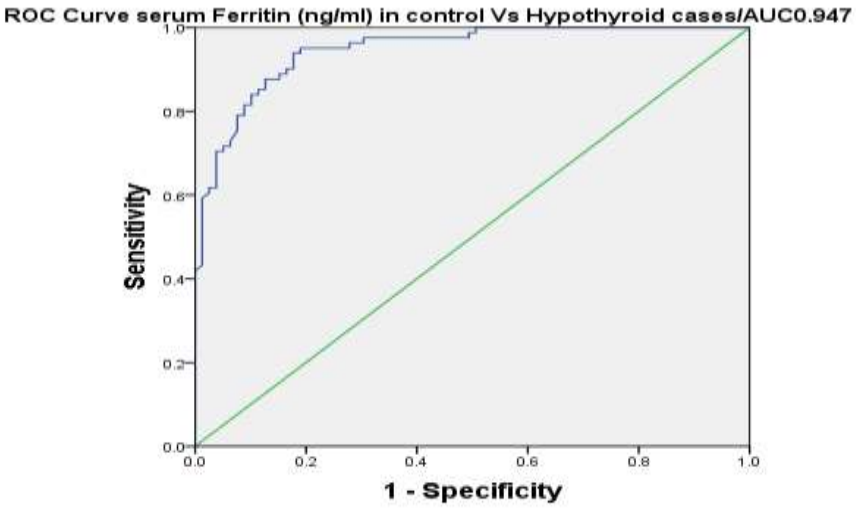

Fig-3: ROC curve analysis of serum ferritin concentration (ng/ml) in hypothyroid and control group

DISCUSSION

In recent years various research has carried out to find the association between serum ferritin and thyroid dysfunction as because iron and thyroid hormone metabolism are interrelated. Iron in the storage form of ferritin plays a vital role in the body's energy expenditure and metabolism.11 The present study aims to evaluate the relationship between serum ferritin and thyroid profile in autoimmune overt hypothyroid patients. According to our study the mean ± SD levels of serum ferritin level in hypothyroid group was 17.15±9.44 ng/ml and in control group was 73.13 ±44.46 ng/ml which clearly suggest that in our study the hypothyroid group had significantly lower level of serum ferritin in comparison to control group which was statistically highly significant with p value <0.0001. Similar finding was reported by Kumar et al.(2017), where they found mean± SD of serum ferritin in hypothyroid group was 12.30±4.94 ng/ml and in control group was 48.10±15.60.16 Sinha, M. K et al. (2022) studied the correlation between vitamin B12, folic acid and ferritin with thyroid hormones in hypothyroidism and found that ferritin was significantly decreased in hypothyroid cases as compared to normal .11 Another study by Niko Rostaei Rad et al.(2016) revealed the relationship between thyroid hormone levels and iron levels in Iranian hypothyroidism patients and they further reported that serum ferritin level was significantly lower in hypothyroidism group, which indicated direct correlation of thyroid hormones with iron metabolism.17 Several other studies also revealed the similar results and they documented a strong association between thyroid hormones and ferritin expression which support our findings. 12,18,19 Studies suggest that thyroid hormone may regulate the

expression of ferritin by regulating iron regulatory proteins (iron responsive element binding proteins, iron response factor) 20 These links between thyroid hormones and ferritin expression probably suggest that a positive correlation exist between the levels of thyroid hormones and serum ferritin in hypothyroid subjects. On the other hand, thyroid hormone production can be altered by low circulating ferritin concentration because decrease ferritin level can reduce the thyroid hormone synthesis. Low ferritin may affect the process by which dormant T4 hormones are converted to active T3 hormones.16 This process takes place mainly in liver and requires adequate supply of store iron.

The present study highly significant negative correlation was observed between TSH and serum ferritin level (r=-0.68). This finding is in accordance with similar study conducted by Kumar et al. (2017) and Saroj Khatiwada et al. (2016) 16,19

Few studies reported contradiction as there was no association exist between iron metabolism, serum ferritin level and thyroid hypofunction. The survey by Yavuz et al.(2004) in Turkey reported no relationship between iron status and thyroid hormone levels in school children.21 Another study conducted by Tienboon et al. (2003) in Thailand revealed that thyroid hormones of children before and after iron treatment were not significantly different from control group. So there was no association exist between iron status and thyroid profile.22

Limitation of the study: Limitation due to small sample size and few parameters were analyzed and very less data was available in autoimmune hypothyroidism. The study was limited to Awadh region (Ayodhya) only. So a prospective research with larger sample size and multicentric study could obtain wider insights.

CONCLUSION

The present study observed that in autoimmune hypothyroidism serum levels of ferritin significantly reduced in comparison to healthy control group. We also found negative correlation between serum ferritin and TSH hormone. Though various studies showed similar results but no study conducted on autoimmune thyroid dysfunction. This current study will furnish helpful insights into the interplay between thyroid hormone function and iron metabolism. Hence early detection of serum ferritin and other hematological parameters must be carried out in autoimmune hypothyroid patients. This valuable information will potentially influence the clinicians and endocrinologists in the better management of autoimmune thyroid dysfunctions. Improved understanding of alteration of serum ferritin in hypothyroid patients can lead to more comprehensive and individualized treatment approaches surely improve better patient care and outcome.

Funding statement: No funding provided for the study.

Conflict of Interest : Author declare no conflict of interest.

Authors contribution: Mohua Roy Mukherjee conceived the study and performed the experiments and analyzed the data and prepared the manuscript. Dr Anupama Sharma guided in writing the manuscript and corrected and edited the manuscript. All other author reviewed and approved the final manuscript.

Acknowledgement: I would like to express my sincere gratitude to my Guide Dr. Anupama Sharma mam and Nims University Jaipur for overall guidance and giving us the platform for our research work. I would like to extend my heartfelt appreciation to my co guides Dr. Manish Kumar Mishra and Dr. Virendra Verma for their invaluable contributions to the data collection process. The research facilities and infrastructure provided by RDASMC, Ayodhya have played a significant role in the successful completion of this study. I am also indebted to the support staffs of RDASMC, Ayodhya who facilitated the smooth operation of our research activities.

Availability of data: The data will be available on request by the corresponding author.

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